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# Rare Earth Elements: Review of Medical and Biological Properties and Their Abundance in the Rock Materials and Mineralized Spring Waters in the Context of Animal and Human Geophagia Reasons Evaluation☆

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ABSTRACT

New data on the abundance of rare earth elements (REE) and their biological properties, which appeared in recent decades, force the researchers to reconsider the facts previously collected by different researchers related to the study of the geophagia phenomenon in animals and humans. From the standpoint of the new data it becomes apparent that one of the reasons for instinctively traditional form of geophagia, as well as for drinking water from mineralized sources by animals and a man with lengthy visits to the same places could be an instinctual drive of a specific organism to adjust in their bodies and tissues the concentration and ratio of the rare earth elements which are able to actively influence, either directly or indirectly (through the effects on metabolism of other chemical elements in the body) the biochemical and physiological processes that determine the quality of health. Since REE influence at the level of nerve tissue biochemistry, hormonal regulation of the body and even at the genetic level, it all can point to a higher order which they occupy in the hierarchy of elements in the composition of any organism. It seems that REE have reasons to claim to be the main causes of all instinctive forms of traditional geophagia and related consumption of mineralized water.



## Brief Overview on Rare Earth Elements Abundance

Rare earth elements group (REE) accounts for 17 representatives including lanthanum and lanthanoid elements as well as scandium and yttrium. Such metals are not as rare as it may seem. Rare earth elements' reserves in the Earth crust are twice as much as stannum reserves, 10 times as much as lead, 50 times as much as molybdenum, and 165 times as much as wolframium. They are 1600 times as much as silver and 3200 as much as gold. Average concentration of lanthanoid elements in the Earth crust is comparable to that of iodine, cobalt and selenium which serious geochemically conditioned human and animal endemic diseases are blamed on. The most frequent rare earth elements are lanthanum and cerium, and the least frequent—thulium and lutetium.

Lanthanoid elements are very similar to each other in physical and chemical properties which can be explained with peculiarity of their electron shells structure. Ionic radiuses of lanthanoid elements expectedly decrease consistently from lanthanum to lutetium. It is related to the fact that when order number increases inner electronic orbits rather than outer ones are built up

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which results in decrease of ions volume instead of its increase. Depending on the degree of difference in ionic size of rare earth elements their isomorphous replacement often takes place. That is why they almost always occur together in nature. They are easy to form combined oxides, halides, phosphates, sulfides and fluorides.

According to Balashov (1976), maximum content of REE among volcanic rocks is characteristic of kimberlites, some kinds of carbonatites, alkali-basalts and granitoids including rhyolites. However, it should be noted that their selective accumulation is common for such type of rocks. For example, with alcalic rocks and postmagmatic products related to them the ceric sub-group develops predominantly; and with postmagmatic products of granitoid rocks with hyperalkalinity—the yttric sub-group.

Expressed differentiation of rare earths can be noted in exogenetic environment. Thus, for example, latheritic crusts of weathering of basalts, limestones and granitoids contain much more REE than parental rocks (Yuangen et al., 2000). All clayish crusts of weathering, especially kaolinic ones, are characterized with enrichment with light REE which is noticed in Africa, for instance (Nyakairu et al., 2001).

According to the Chinese researchers' experiments (Zhicheng et al., 1994), soil organic matters may easily wash REE out of parental rocks, carry them in the complex form and re-deposit them in the subsoil levels among soil organic matters and clays. Any acid waters including hydrocarbonate and sulfate ones (Vakh, 2012) also may easily wash out REE from soil. In such event these waters are enriched with one set of REE and the rocks washed by them—with the other set of REE. Also, it has been already discovered that REE content in the soils under the humid climate conditions can be very low, considerably lower than bulk earth values (Vodyanitski & Savichev).

Background level of REE content in waters, both surface and subsoil, varies significantly and depends mostly on respective territory rocks enrichment with such elements. In such a case intensive concentration of REE in subsoil waters occurs in the areas of active water exchange which is caused by processes of their leaching from parental minerals. Mineralized waters of carbonaceous mineral springs are especially rich of REE (Kharitonova, 2013).

For instance, REE concentration in the surface and fresh waters of the South of the Russian Far East varies between 0.1 and 1.3 μg/l. In this respect the highest concentration (0.48–1.3 μg/l) is characteristic of the rivers and underground waters, catchment basins of which are located within Sikhote-Alin volcanic belt; the lowest concentration—in the waters of the Western Sikhote-Alin region where mostly sedimentary rocks occur (0.09 μg/l). It has been determined also that profile of REE abundance in fresh waters of different areas of the region is uniform and characterized with Ce deficiency and enrichment with REE of the middle group (Vakh, 2012).

As for underground mineralized carbonaceous waters (most frequent in nature), according to the research of six such basins in the south of the Russian Far East, REE concentration in them fluctuated between 0.36 and 25 μg/l, and depended considerably on composition of the enclosing rocks. Maximum concentration has been found in volcanogenic rock formations, minimum—in the sedimentary ones. At the same time mineral waters of each basin have their specifics of REE abundance (Kharitonova, 2013).

All the facts are presented only to emphasize that some rocks, soils and natural waters may be either greatly enriched or depleted with rare earth elements. However, geography of contemporary landscapes with the most contrastive REE abundance is limited mainly to subequatorial areas of the Earth.

Lanthanoid elements are found in the organisms of representatives of almost all worlds of wildlife: in bacteria, archaebacteria, fungi, vegetables and animals. Lanthanoid elements may be confidently determined in all organisms with neutron activation methods of analysis and, moreover, in all biological tissues and fluids including human ones—in all organ tissues, endocrine glands, hair, bones, nails and all biological fluids. According to Ignatova (2010), all systems of human organism can be distributed pursuant to the following scheme on the basis of their REE accumulation level (towards decrease of concentration): respiratory, endocrine, digestive, integumentary and locomotor, genitor-urinary systems, blood and lymph circulation systems, cerebrospinal nervous system. Most REE are accumulated in the organs of respiratory system, spleen, adrenal glands and skin.

Lanthanoid elements content in the human organs and tissues, as well as in the ignition residues of the whole body, reflects landscape–geochemical and ecological–geochemical peculiarities of the regions where the human lives. Data obtained by Brown et al. (2004) demonstrate this fact very well. They compared La and Ce content in deciduous teeth of children from Uganda and the Great Britain. Teeth from Uganda showed La concentration 4 times as much as teeth from the Great Britain, and Ce concentration in children's teeth from Uganda was almost tenfold as higher compared with the teeth from the Great Britain.

Relation of lanthanoid elements concentration in the body with concentration of such elements in the environment is clearly demonstrated in China, in the areas of REE mining. Concentration of the elements was determined in the hair of 118 local residents in the neighborhood of one of such enterprises in Chinese Inner Mongolia (Wei et al., 2013). It was found out that average REE concentration in the hair of both men and women started to increase upon the enterprise opening. At the same time average content of light REE (La, Ce, Pr and Nd) in the hair of mine workers was significantly higher than that in the hair of people who were not the enterprise employees. According to the data based on age groups, bodies of men and women under 60 years accumulate mainly light REE. At the same time concentration of heavy REE in the bodies of men who were not exposed to technological impact decreases with aging.

According to the other cycle of studies carried out in the area where Chinese REE mines are located, REE concentration in the local residents' blood varied between 424.76 and 1274.80 μg/l, in their hair—between 0.06 and 1.59 μg/l. However, it was found out that average REE concentration in local water wells was 50 times as much as compared with drinking water of Fuzhou (Li et al., 2013).

Lanthanoid elements are permanent components of human milk. Thus, when studying human milk of women-residents of Tomsk (Stankevich et al., 2013) the content of La, Ce, Sm, Yb, Lu, Tb, and Eu was established. Also, it was revealed that their concentration in human milk not only varied for women from different districts of the city but also changed depending on the duration of lactation cycle.

Presence of La, Ce, Eu, Gd and Ca has been determined in men's sperm (Marzec-Wróblewska et al., 2015). Also, both positive and negative associations of such lanthanoid elements' concentrations with sperm qualitative parameters, ejaculate volume, sperm cell density, their motility and morphology were found. La, Ce and Gd concentration in sperm was discovered to be positively associated with progressive motility of sperm cells and percentage of normal sperm cells and simultaneously to be negatively associated with sperm cells density.

Lanthanoid elements are permanent components of phosphate and oxalate kidney-stones. Phosphate kidney stones are characterized with inconsiderable positive anomaly of cerium and enrichment with heavy REE (Koeberl & Bayer, 1992). Authors of this research focus on the fact that natural non-biogenic apatites are enriched with light REE. Besides, all phosphate kidney-stones and sometimes oxalate kidney-stones showed minimal quantity of samarium which is also unusual as compared with non-biogenic phosphates.

Lanthanoid elements are actively accumulated by some kinds of bacteria. For example, Japanese researchers (Takahashi et al., 2005), who studied rare earth elements adsorption on the cell walls of bacteria *Bacillus subtilis* and *Escherichia coli*, determined that such elements as Sm and Eu had maximum adsorption on the cell walls. Some enrichment was pointed out for Pr and expressed decrease of Nd sorption. Other cycle of studies (Takahashi et al., 2007) showed that *B. subtilis*, *E. coli*, *Faecalis alcaligenes*, *Shewanella putrefaciens* and *Pseudomonas fluorescens* demonstrated expansive growth of heavy REE with weak peak approximately in the middle of their spectrum. Results also reveal clearly that different kinds of bacteria are characteristic of their own patterns of REE accumulation.

Some microorganisms are found out to adapt to extreme conditions of living with the help of lanthanoid elements. So, T. Barends and colleagues (http://ria.ru/studies/20131031/973948225.html?ria= tmjg1hqsfn2rsf5t4t67rh36movuouqm#ixzz3WieEPWNA, .) discovered bacterium *Methylacidiphilum fumariolicum* in the waters of acidic hot spring (pH of water is between 2 and 5, t is about 60 °C) in the vent of volcano Solfatar, Italy. Upon studying the structure of methanoldehydrogenase enzyme of the bacterium the researchers found out that it includes rare earth elements La, Ce, Pr and Nd rather than calcium as most methane oxidizing bacteria and that it takes these elements from the environment. Also researchers discovered that similar structure of methanoldehydrogenase is characteristic of different kinds of bacteria which inhabit coastal waters and leaves of the plants. Thus, they made a conclusion that such bacteria may be widely distributed.

## Medical and Biological Properties of Rare Earth Elements

We have just started studying lanthanoid elements biological functions. However, even the known data give us grounds to believe that such elements play an unusually important role in structure and functioning of any biological system.

For instance, lanthanoid elements are known to function as calcium analogs in the biological systems. Trivalent lanthanum ions may substitute calcium in many proteins including enzymes (Brittain et al., 1976; Martin & Richardson, 1979) and cell membranes (dos Remedios, 1981; Mikkelson, 1976). Lanthanoid elements may cause damage of blood lymphocytes chromosomes (Xu et al., 2000) and hepatic impairment (Nakamura et al., 1997; Salas et al., 1976; Tuchweber et al., 1976). At the same time it was determined that gadolinium ions, like praseodymium ones, selectively inhibit the function of Kuppfer cells on the liver tissue cultures and weaken activity of cytochrome P450 in the hepatocytes, thereby protecting hepatic cells from toxic products of xenobiotics biotransformation (Palasz, 2000). Lanthanoid elements' ions are capable to regulate transportation and releasing of synaptic transducers in the neuronal cells and to suppress some membraneous receptors such as $GABA_A$ and NMDA (glutamate) receptors, to influence rate of learning and memory capacity (Li et al., 2000). It has been already established that REE may affect both cell mediated and antibody mediated immunity (Liu et al., 2000; Wang et al., 1995; Wei et al., 2000; Zhang et al., 1993). Tests on rats showed that cerium may weaken hemoglobin capacity to combine the oxygen (Cheng et al., 2000). Also, it was determined that trivalent La ions may change expression level of some kinds of genes which was proven on hepatocytes (Zhao et al., 2004) and cells of *E. coli* bacteria (Wenhua et al., 2003).

Tests on rats demonstrated that the chronic effect of lanthanum chloride caused disorders of homeostasis of minor constituents, enzymes and neurotransmitters in brain (Feng et al., 2006). For instance, it was established that distribution of such elements as Ca, Fe and Zn in the brain was considerably changed upon exposure to lanthanum effect. Besides, lanthanum chloride in the quantity of 40 mg/kg considerably inhibited activity of $Ca^{2+}$-ATPase. Functions of central cholinergic system were also obviously impaired: content of some monoamines mediators decreased significantly. Other group of researchers obtained similar results but using yttrium salts (Jiesheng et al., 2002). Mice were given water with trivalent yttrium ions in different concentrations during seven months and levels of minor constituents (Cu, Zn, Mn, Fe, Mg, Ni and Co) in the mice's brains, parents and first generation were monitored. It was revealed that pattern of minor constituents in the brain had been changed severely as compared to reference sample. Levels of Fe and Ni decrease significantly and the level of Co increases. Supposition was made that Y may have an effect on metabolism and distribution of some minor constituents in the brain which may result in a change of physiological functions.

Special affinity of lanthanoid elements to neuronal cells was proven not only on brain tissues but spinal cord tissues too. Injection of single dose of nanocerium (10 nm) at the moment of rat spinal cord cells inoculation contributed to much higher neurons survival as compared to reference culture (Das et al., 2007). Following the results of the oxidizing trauma test upon treatment of spinal cord cells with hydrogen peroxide, survival level of the cells treated with nanocerium was also significantly higher.

According to the other group of researchers (Dowding et al.), cerium nanoparticles may be consumed by neurons and accumulated in the mitochondrial, outer and cytoplasmic membranes. Besides, nanocerium reduces level of nitrogen and tyrosine protein active forms in the neurons affected by peroxynitrites.

It is commonly known that fast and effective wound healing requires coordinated action with participation of fibroblasts, keratinocytes and vascular endotheliocytes. Experiments (Chigurupati et al., 2013) showed that local application of watersoluble cerium oxide nanoparticles accelerated healing of the whole thickness of mice's skin wounds with the help of mechanism which activates intensification of proliferation and influx of fibroblasts, keratinocytes and endotheliocytes.

There are reliable data that lanthanoid elements may, to a great extent, determine functioning of the endocrine sphere, including influence over functioning of thyroid gland and hypophysis, and accelerate or suppress growth hormone production (He et al., 2003). Analysis of thyroid gland elemental composition demonstrated (Denisova et al., 2010, 2013) that such organ is an organ-carrier of many minor constituents and simultaneously an organ-accumulator of a number of rare elements including La and Sm. Under pathological conditions of the organ Ce, Lu and Yb are found additionally among the lanthanoid elements.

Animal experiments repeatedly confirmed lanthanoid elements effect on endocrine sphere especially on the rate of the organisms' growth. It was proven not only by experiments but also in the course of fattening process. Chinese livestock farmers effectively use REE based growth stimulating substances for a long time. In the meantime, positive effects were detected almost for all kinds of livestock animals. Since 1999 Animal Nutrition Institute in Munich has begun research of REE application for animal breeding in European countries. Following the results of such research first growth additives were permitted for application in Switzerland (Rambeck & Wehr, 2005).

Below, to avoid overcharging of the text, we will point out only several experiments which are the most interesting for us. Thus, experiment on pigs (Wang & Xu, 2003) was carried out on two groups, 30 animals in each. One group was fed with addition of 100 mg/kg of La salt, the other served as a reference one. Blood was constantly tested for growth hormone level. Results showed that average daily gain and feedstuff utilization coefficient increased in the experimental group by 12.95% and 6.78% respectively. Blood sample analysis revealed that maximum peak and average level of growth hormone in blood serum of the experimental group pigs were higher by 80.42% and 64.91% respectively. There was no difference in respect of La content in the organs of experimental and reference groups of animals. Similar results were described earlier (Cheng et al., 1994; He & Xia, 1998; Li et al., 1992; Zhu et al., 1994). Very close results were obtained by German researchers (Schramberg, 2004). Average daily gain of their piglets reached 22.6%, in the meantime, the group with low La dose did not demonstrate any gain. Simultaneously they carried out an experiment to determine REE influence over fermentation processes in the imitative scar. Effect of various doses of REE was compared with reference sample (without additive). Each test lasted for 10 days. They determined REE additives effect on the following properties: pH, $NH_3$, oxidation–reduction potential, fatty acids spectrum and gas production level. It was discovered that REE additives did not influence fermentation pattern in the scar.

Data obtained for pigs are in a good agreement with the results of rat and broiler experiments (Halle et al., 2002; Nakamura et al., 1997, 1991b; Xie et al., 1991).

Overdosage of lanthanoid elements when given to the animals orally causes decrease of their growth and other negative impacts. For example, when adding 20 mg/kg of La to the rats' feed their growth was significantly inhibited, levels of white corpuscles, thrombocytes and reticulocytes in blood were reduced (Cheng et al., 2014). Besides, liver function was impaired: high level of alanin aminotransferase, total bilirubin, biliary acid and triglycerides, low glucose content and albumin and globulin ratio. Also, there was observed a damage of cytoarchitechture and fatty liver syndrome. It was revealed in the course of the experiment that trivalent Ce ions had higher toxicity than La and Nd ions.

Enormously important property of lanthanoid elements has been recently discovered in virology. Experiments with cell cultures showed that some lanthanoid elements can block capability of the host cell to support RNA replication of flaviviridae (Wengler et al., 2007). Flaviviridae family includes 53 human and animal viruses, which are passed mainly through arthropods (mosquitoes, acarian). The most typical of the viruses are yellow fever virus, West Nile virus, dengue virus and tick-borne encephalitis virus. The experiment showed that upon the cell treatment with La ions within 30 days changed their cytochemistry so that such cells would never support flaviviridae replication. Moreover, such changes occur in the cells treated before infection, during and after infection. Such changes occur in the cells of Vertebrata and Insecta. The experiment revealed also that lanthanoid element ions' activity decreases when ion diameter becomes less. Only four ions with the largest diameter are capable to induce immunity to viruses in the cells of Vertebrata effectively, La and Ce ions being the most effective. Researchers point out that if suitable route of lanthanoid elements ions entry is developed effective drugs for treatment of all kinds of diseases caused by flaviviridae may be created.

All the facts about biological properties of lanthanoid elements mentioned above convey the suggestion that both excess and deficiency of such elements in water and soil should have a significant impact on human and animal health. First information on possible existence of endemic diseases directly related with REE appeared in early 1990s in India.

Presence of Ce high level in nutrition and lack of Mg in the southern part of India were established as a potential ecological factor of Loeffler endomyocardial fibrosis etiology (LEF) (Sliwa et al., 2005).

The disease was first described in 1946 in Africa and is most frequent in tropical and subtropical areas all over the world. In Africa the disease occurs in Uganda, Kenya, Tanzania, Mozambique, Gabon, Kongo, Cameroon, Sudan, Nigeria, Cote d'Ivoire and Ghana. Localization of the disease in Africa first of all is typical for tropical forest areas and mainly occurs among rural people and farmers. It should be pointed out that in Uganda the disease is more frequent among immigrants from neighboring Rwanda and Burundi who settled in certain geographic areas [Gene Burkman 2008]. Among other regions with high level of disease occurrence there are some countries of South America (Brazil and Colombia), many cases were registered in southern China (Guangxi province) (Bukhman et al., 2008).

Signs of chronic LEF manifest themselves as cachexia, shortened fingers and toes, and growth inhibition. Men demonstrate testicular atrophy and poor development of secondary sexual characteristics which, as commonly believed, are the results of long-lasting weak cardiac output. Some patients except for fibrosis of myocardium have fibrosis of skeletal muscles including their atrophy. Most patients are registered to have cardiac failure, arrhythmia and thromboembolism (Mocumbi, 2012).

Clinical features of the disease depend on the stage and degree of heart destruction. Up to 50% of children and teenagers point out that the disease starts from fever, shivering and facial oedema. The disease may disappear or may result in fast development of cardiac failure and early death. Most professionals tend to think that Loeffler endomyocardial fibrosis is a constitutional inflammatory disease (Sliwa et al., 2005). Initially, infecting with some viruses or Haemamoebas including malaria parasite as the responsible triggers of the disease was the most popular version (Sliwa et al., 2005). Later, on the basis of the data obtained in India, most researchers started to believe in geochemical version of the disease occurrence.

Even the very first study of cerium influence over collagen synthesis in the culture of cardiac fibroblasts and explants with concentration found in the cardiac tissue of the patients revealed stimulating effect of cerium on collagen synthesis and its accumulation typical for endomyocardial fibrosis (Shivakumar et al., 1992). Later, the results were confirmed with experiments on rats (Prakash Kumar et al., 1995; Kumar & Shivakumar, 1998) and rabbits (Kartha et al., 1998) whose feedstuff had low content of magnesium and high content of cerium.

Recently studies have been carried out to determine area of the most frequent occurrence of LEF in India (Raman Kutty et al., 2015). Four zones near the coast line were found within 3 districts in the south and south-west India. There are large monazite sands deposits known in two of them (Ce, La, Nd and Th phosphates). However, all the territories are not related to the occurrence of filariasis and eosinophilia which had been earlier thought to cause LEF in India. All the facts contribute to geochemical version of the disease nature. Similar studies carried out in Uganda (Smitha et al., 1998) showed that in such an endemic in respect of LEF area of the world cerium is not included into monazite sands but is contained in the form of secondary minerals within the particles of 20 μm size which occur in the soil and subsurface grounds.

Relation between scandium content in nails and risk of acute myocardial infarction was appraised within the study with 10 medical centers of Europe and Israel being involved. Scandium content in the nails was determined by means of neutron activation method for 684 patients with heart attack and 724 healthy persons at the age of 70 years and younger. Average concentration of the element in the experimental group was 6.74 μg/kg and 7.75 μg/kg—in the reference group (Gómez-Aracena et al., 2002). Cerium content was measured in the nails within the similar experiment with the same patients involved. In the meantime, cerium average concentration for the patients turned out to be 186 μg/kg and for the reference group—173 μg/kg (Gomez-Aracena et al., 2006). As a result a conclusion is made that scandium protects the organism from coronary heart disease somehow and cerium excess, on the contrary, may be one of the factors for the disease development.

So, we have determined that lanthanoid elements are distributed in the landscapes very unevenly, at the same time they rather significantly and specifically influence over biological chemistry and physiological processes in the living organisms of almost all representatives of living nature including animals and human beings.

## Rare Earth Elements and Geophagia

New data on abundance of rare earth elements and their biological properties presented above make us revise facts collected earlier by different researchers in respect of studying of geophagia phenomenon among animals and human beings. I would like to emphasize that what is meant here is instinctive form of geophagia which has been taken place in the same locations for hundreds and thousands of years. This study excludes rare non-systemic cases of instinctive geophagia as well as occasional eating of soils and grounds by animals together with their main feed or drinking water, and artificial additional feeding with mineral substances.

The most popular supposition in respect of geophagia reasons has been "mineral supposition" (on additional mineral nutrition). This supposition came to the minds of all those who tried to reflect on the reasons why animals inhabiting certain regions (and sometimes human beings also) seek to eat lithogenous mineral-crystalline substances only in particular places from time to time and to drink mineralized water from springs spatially linked with such substances. Today this mineral supposition is divided into two components: one is related to need for sodium revealed for many animals long ago, and another—to imbalance of some other elements in the organism, and in this case there may be either deficiency or excess of elements in the organism.

As for the sodium component of mineral supposition it is deemed to be quite proven at least in respect of the cases when we deal with large herbivores, with higher concentration of bio-available sodium ions or salts being found in the eaten grounds as compared to analogous background formations. In other words, search for sodium is considered to be one of quite proven and commonly recognized reasons of geophagia. Seeking of natural permanently existing sources of sodium explains at least part of geophagia manifestations among animals. We will return to sodium component of mineral supposition below and meanwhile let us move to its other components.

As for targeted search for the elements other than sodium in the consumed grounds and waters, for the present, iron was most frequently considered as the element-candidate. This includes all the cases when human or animal geophagia was accompanied with obvious signs of iron deficiency or fairly increased need for such element and when excess of iron was found in the eaten grounds.

For example, according to V.S. Makheiny and colleagues (Mahaney & Hancock, 1990; Mahaney et al., 1990), it is iron deficiency which explains frequent occurrence of geophagia among primates, buffaloes and other hoofed inhabiting Africa on the sides of such mountains as Kenya or Virunga at the height of between 2000 and 3000 m. It is explained by the fact that there is a lot of iron in the eaten grounds and the provision of body tissues with oxygen depends greatly on the element, on its content in blood within hemoglobin, as one starts feel deficiency of oxygen in the air at such a height.

For the present, obvious (manifested with symptoms) and instrumentally confirmed signs of iron deficiency related to need for geophagia were revealed only for human beings. Relationship of human geophagia with anemia signs was pointed out as early as in the beginning of I millennium by Cornelius Celsus, the Roman healer (quoted according to Selinus et al., 2010). Since that time relationship of human geophagia with anemia signs was repeatedly confirmed in different parts of the world. To avoid overcharging of the text with the facts we will give only one example of geophagia traditions research in the vicinity of Shiraz, Iran, which A. Prasad and his colleagues were studying for a long time (Prasad, 1992, 1989). As early as in the beginning of 1960s he reported that he observed hypochromic anemia syndrome of many rural people in the vicinity of Shiraz. Also, he described cases of dwarfism, brachydactyly and poor development of some men's primary and secondary sexual characters. In this case eating of clays is very popular among local inhabitants. Later A. Prasad explained (Prasad, 1991) that cereal crops with high content of phosphates was the main component of diet of people inhabiting such areas and this negatively affected ferrum-zinc balance in their bodies.

It is worth mentioning that many studies devoted to geophagia issues tell about signs of anemia of people addict to geophagia including those having a lot of diagnoses identified beginning from “Cachexia Africana” to “sickle cell anemia”. Such cases are summarized, for instance, in the following works (Campuzano Maya, 2011; Collignon, 1992; Selinus et al., 2010).

First mass cases of “Cachexia Africana” and geophagia related to them were described as early as in the beginning of XIX century by colonial doctors for field hands of South America (Brazil, Jamaica, Surinam). Among the most well-known descriptions there is a colonial doctor's article (Cragin, 1836), where the following main symptoms of the disease are specified: fever with irregular intervals, excessive sweating, swollen and lustrous face and upper and lower extremities. Conjunctiva of eyes becomes particularly snow-white. Lips and gums are light, sometimes with marble stains. Rapid heartbeat with weak pulse. Liver and spleen are often enlarged. Lymphatic glands are swollen.

I mentioned those symptoms deliberately because they are in a good agreement with the symptoms found later by A. Prasad for people who ate clays in Iran as well as with the symptoms of systemic disease named endomyocardial fibrosis and which, as it is already known, is directly connected with REE concentration and composition in the body including myocardium.

Below we present experimental data which do not confirm direct relationship between geophagia and removal of iron deficiency, as well as zinc, calcium and other elements deficiency. Such experiments are reviewed in the study of S.L. Young et alias (Young et al., 2011). Below there are some of them, most representative ones.

Thus, a number of researchers (Nchito et al., 2004) were giving iron preparations and multivitamins to 402 Zambia schoolchildren with anemia addict to geophagia for 10 months. As a result the authors made a conclusion that neither iron preparations, nor multivitamins with minor constituents were effective insofar as it concerns elimination of their addiction to geophagia in spite of improvement of the patients' blood indexes.

A remarkable experiment was carried out on pregnant rats which were fed with clay (Edwards et al., 1983). Twelve pregnant female rats and later their offspring (totally 88 animals) were divided into three groups: reference group, group with a diet containing 20% of clay, and group with a diet containing 35% of clay. Experimental feedstuff was given to adult rats during pregnancy and within 14 days upon delivery. As a result, values of hemoglobin and number of red corpuscles of mother-rats and infant-rats in all experimental groups did not vary from the corresponding values of the reference group.

Other group of researchers (Dreyer et al., 2004; Hooda et al., 2004; Seim et al., 2013) also proved through experiments on rats that not only iron but zinc and copper contained in the clays used for geophagia were little or not available for organisms. Moreover, many clays used for geophagia during the experiment distinctly worsened absorption even of iron which was brought to the digestive tract with feedstuff.

Supposition that pregnant women use geophagia as a method of iron, zinc and calcium replenishing was also recognized as unconvincing. Upon carrying out of observation over geophagia among pregnant women in Africa (Institute of Medicine, 2002) it was reasonably pointed out that real pregnant women's need for iron, zinc and calcium does not coincide with the time of their maximum thirst for geophagia. Geophagia peak among pregnant women fell mainly on the beginning of pregnancy. While at early stage of pregnancy women should desire to consume less iron than during the previous period when they regularly go through menstrual blood loss and far less than at the late pregnancy stage due to the baby's development needs. In the beginning of pregnancy women should have significantly less need for calcium as most part of calcium used for the baby's needs is accumulated during the third trimester. As for need for zinc it does not change notably during the whole period of pregnancy (Institute of Medicine, 2002). These facts indicate that reasons of clay eating by the pregnant women are not connected directly with the replenishing of mineral components under examination.

Hereafter we will pay attention to minor constituents, the lack or deficiency of which in the environment has an effect on endemic microelementosis occurrence. Again zinc, selenium, molybdenum, iodine, bromine, cobalt, copper and others can be found among elements which are mentioned in studies discussed in respect of geophagia.

In respect of such suppositions it should be pointed out that no case concerning geophagia within the studied context, has been confirmed reasonably. In 1977 at the time of soviet geochemical ecology school prosperity I had a chance to talk to Victor Vsevolodovich Kovalskiy, the most famous leader in the sphere. The great scholar of geochemistry was very interested in my description of geophagia facts which I had observed and studied among animals in Sikhote-Alin by the time, but he could not remember any fact from his long-term researcher's experience which would reveal relationship between animal geochemical endemical diseases and their urge to eat rocks.

Other great geochemists, I had a chance to talk to, showed similar reaction for geophagia facts. Among them were A.I. Perelman, the prominent theoretician of landscape geochemistry, and V.V. Ermakov, biogeochemist who had studied human and animal endemic microelementosis in the Russian Far East for many years.

Consequently, there is still no reasonable set of facts to confirm relationship of animal and human geophagia with typical microelementosis. At the same time the relationship of geophagia with endemic diseased conditions and heart and blood diseases, connected directly or indirectly with REE, gains more and more confirmation.

It is well-known that places where wild animals eat rocks are often located near or around water sources. We started hydrochemical research of such water sources in Sikhote-Alin in early 1980s (Panichev, 1990), when our analytical capabilities did not allow us to determine REE content in water. Nevertheless, we took water samples from 45 water sources which were regularly visited by animals and identified main hydrochemical parameters of them: pH, total salt content, and basic ions' composition. According to the main anion composition, they all turned out to be hydrocarbonate. According to cations composition, approximately half of them turned out to be sodium, and the other half—sodium-calcium. pH varied between 7.05 and 9.1. Total salt content varied between 0.2 and 1.5 g/l. In the meantime, animals preferred most of all the water from the sources with salt content about 0.5 g/l. All the water sources visited by the animals had direct or indirect signs of connection with tectonic fraction zones. Part of them situated among volcanic rocks and the other was surrounded with sedimentary rocks but simultaneously not far from the boundary of volcanites field.

It is worth mentioning that on the territory of contemporary continent of North America pursuant to the data of a number of researchers (review of their studies is presented under Panichev, 2011) animals visit similar mineralized water sources according to both exterior signs and chemical composition.

According to recent research of such source waters in Sikhote-Alin (Kharitonova, 2013) most of them showed maximum REE concentration as compared to the surface waters, strongly mineralized and salt underground waters enriched with heavy REE sometimes having anomalous concentration of samarium and europium.

The fact that there are high REE concentrations in low-mineralized hydrocabonate-sodium source waters within areas of volcanic and igneous-sedimentary rocks spreading discovered by the researchers gives reasons to believe that animals seek drinking at least part of such waters not for the sake of sodium ions but for the spectrum of lanthanoid elements contained there and, perhaps, combined with other minor constituents. It is difficult to believe that animals are ready to overcome 30 Km and more only for the purpose of drinking half a bucket of water where less than a teaspoon of sodium bicarbonate is dissolved. On the other hand, animals' capability to feel and distinguish sodium ions in water and wet grounds from many other ions at least approximately explains the mechanism of search for the elements required for a body. In the meantime, it is worth mentioning that even animals' mechanism of sodium identification is not strictly specific. Experiments proved that animals could confuse sodium salts with lithium ones. They eat them in the same way as sodium salts and stop only when they feel symptoms of toxic effect (Blair-West et al., 1968).

If we suppose that animals can intentionally look for rare earth elements in the rocks and waters immediately arises the question on what the mechanism of their identification is. It seems to be the most difficult question for serious perception of the idea on “rare earth” reason for geophagia. Moreover, if this reason is used to explain most cases of traditional forms of such phenomenon. An interesting discovery has been made recently which, on my opinion, gives grounds to hope that this difficult question is likely to have decision.

Thus, it was established that sand dollars (*Echinodermata* and *Echinoidea*), widely spread representatives of sea benthos, inhabiting coastal waters, are capable to accumulate in special diverticula of their digestive tract mineral grains of exceptionally two minerals—zircon and ilmenite with apparent preference to zircon (Elkin et al., 2012). In the meantime, it was established that content of minerals required to the sand dollars in the quartzo-feld spathic sand constitutes maximum 0.02% for zircon, and maximum 0.08% for ilmenite. The researchers supposed that the animals identify minerals on the basis of their specific weight because two minerals have almost equal specific weight, however, it is significantly more than a specific weight of quartz and feldspar. No one managed to explain why sand dollars who spend most part of their lives dug into the sand should recover ballast of zircon with very great difficulties. The fact that number of zircon grains is four times as less as number of ilmenite grains, with ilmenite being heavier, also contrast with the supposition of “ballast”. The need for zircon may be explained, on my opinion, by the fact that the animals search for them on the basis of their REE content rather than weight. Indeed, zircon has few competitors in this in the sea sand. Explanation why REE is required for the animals was presented above in general terms. Animals' mechanism of REE identification in natural substances is to be puzzled out. And it is quite possible that sand dollars can help with it.

## Conclusion

Thus, we have found out that new data on REE abundance and their biological properties which have appeared in recent decades allow looking at facts collected earlier by different researchers concerning studying of geophagia phenomenon among human beings and animals in an absolutely new perspective. It is obvious that one of the reasons for animal and human instinctive-traditional geophagia and drinking of water from mineralized sources with longtime visiting of the same places may be instinctive drive of a certain organism to correct concentration and proportion of rare earth elements in its organs and tissues which are capable to influence actively, directly or indirectly (through effect on exchange of other chemical elements in the organism), over biochemical and physiological processes which provide quality of its health. As REE affect through the level of biochemical processes of neural tissues, endocrine control of the body and even on genetical level, all these facts may point out to the higher position they have in the elements hierarchy within any organism. It may follow herefrom that REE can pretend to the rank of main reason for the appearance of all instinctive forms of traditional geophagia and drinking of mineralized source waters related to it.

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